

## Longitudinal Measurement of Renal Oxygenation and Perfusion in Donor-Recipient Pairs Using BOLD and ASL MRI

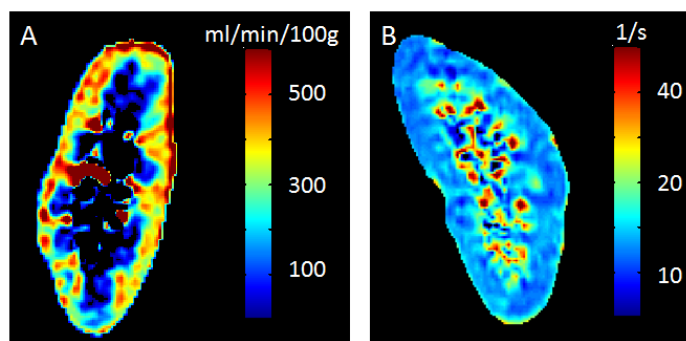
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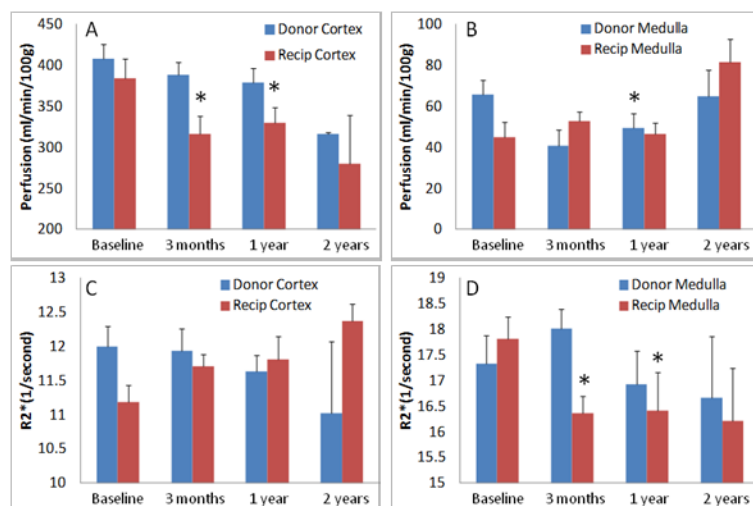
**Introduction:** Routine monitoring of renal function following transplantation is important for early detection of disease. Serum creatinine measurements are commonly used to assess renal allograft function, but this approach has poor sensitivity until late in chronic disease processes [1]. Blood oxygen level-dependent (BOLD) and arterial spin labeling (ASL) MRI are sensitive to tissue oxygenation and perfusion, respectively, and may provide noninvasive means for longitudinal monitoring of functional changes in renal allografts. Although these techniques have been used in short-term studies [2,3], long-term longitudinal studies of allograft function by MRI are currently lacking. Here we present measurements of renal perfusion and oxygenation in donor-recipient pairs up to 2 years post-transplantation as part of an ongoing longitudinal study.

**Materials and Methods: Human Subjects.** This study included 10 recipients of renal transplant and their donors. BOLD and ASL MRI were performed on the donors prior to transplant surgery (baseline) and on both donors and recipients 3 months, 1 year, and 2 years post-surgery. This study was compliant with HIPAA and performed under an IRB-approved protocol. **BOLD MRI.** All images were acquired on a 1.5T General Electric Signa HDx scanner with an 8-channel phased array cardiac coil. BOLD exams consisted of 5 coronal slices acquired with a  $T_2^*$ -weighted multi-gradient-recalled echo sequence and a 16-second breath-hold for each slice (TR/TE/flip = 87ms/7-41.8ms/40°, 16 echoes, FOV = 32-34cm). **ASL MRI.** ASL exams consisted of a single sagittal slice acquired using a FAIR-bSSFP sequence with a 1.2 second inversion time. Respiratory coaching and triggering were used to acquire 32 control-tag pairs (TR/TE/flip = 4.6ms/2.3ms/70°, FOV = 34 cm, slice thickness = 8 mm). **BOLD Image Processing.**  $R_2^*$  maps were generated by fitting the echo images with a decaying exponential function. 5 regions of interest (ROIs) were drawn in the cortex and medulla of the  $T_2^*$ -weighted images and the mean  $R_2^*$  across all ROIs was calculated. **ASL Image Processing.** The 32 control-tag pairs were registered based on normalized mutual information and the average control-tag difference was calculated based on a 1-compartment model and assumed  $T_1$  values of 966 ms in the cortex and 1410 ms in the medulla. Cortex and medulla were segmented by an interactive thresholding technique and average perfusion values in each tissue were calculated. **Statistical Analysis.** A Wilcoxon signed-rank test was used to evaluate statistical changes at 3 months and 1 year relative to baseline. Data at the 2-year time point were not statistically evaluated due to the small number of data (N=2) available at the time of submission.

**Results and Discussion:** Parametric maps of perfusion and  $R_2^*$  are shown in Fig. 1. Perfusion and  $R_2^*$  values at each time point in donors and recipients are presented in Fig. 2. Both cortical perfusion (Fig. 2A) and medullary  $R_2^*$  (Fig. 2D) were significantly lower at 3 months compared to baseline in the transplanted kidney and remained lower than baseline at the 1 year time point, indicating persistent change in renal function. The decline in perfusion may be due to the use of prescribed calcineurin inhibitors or injury during transplantation. The paradoxical result of decreased  $R_2^*$  (implying increased oxygenation) concomitant with decreased perfusion might be explained by a change in tubular metabolism and oxygen consumption. Medullary perfusion significantly decreased between baseline and 1 year in the remaining donor kidney (Fig. 2B), but the explanation for this change is unclear. Continued data collection at the 2-year time point will further examine long-term changes in renal function after transplantation.



**Figure 1.** Typical parametric maps of renal perfusion and  $R_2^*$ . (A) Perfusion map in the sagittal plane showing relatively high perfusion values (yellow/red) in the cortex and low values (blue) in the medulla. (B)  $R_2^*$  map in the coronal plane showing relatively low  $R_2^*$  values (blue) in the cortex and high values (green) in the medulla. Very high  $R_2^*$  values (red) correspond to blood vessels.



**Figure 2.** Renal perfusion (A-B) and  $R_2^*$  (C-D) between baseline and 2 years post-transplantation. Asterisks denote a significant difference ( $p < 0.05$ ) compared to baseline values. Perfusion in the recipient cortex was significantly lower at 3 months and 1 year compared to baseline.  $R_2^*$  in the recipient medulla was significantly lower at 3 months and 1 year compared to baseline, indicating increased oxygen availability at these time points. Data are presented as mean + standard error. N = 10 at baseline, 3 months and 1 year. N = 2 at 2 years.

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**References:** [1] Chapman JR et al. *J Am Soc Nephrol.* 2005. [2] Malvezzi P et al. *Transplant Proc.* 2009. [3] Lanzman RS et al. *Eur Radiol.* 2010.